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Major review

Techniques, indications and complications of corneal debridement

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ABSTRACT

The cornea is the most exposed surface of the eye and, as such, is vulnerable to external trauma and the risk of infection. Many corneal diseases alter shape, surface, and transparency and thus result in reduced vision. The external position of the cornea, however, lends itself to diagnostic and therapeutic maneuvers that are commonly performed and readily done in the clinic. More sophisticated techniques require the use of complex equipment such as excimer and femtosecond laser. Complications that develop from poor healing and/or secondary infection are best avoided with appropriate technique, antisepsis, and modification of wound healing. We review corneal debridement in the management of corneal disease.

1. History

Erasmus Darwin, grandfather of Charles Darwin, was the first in the English literature to suggest therapeutic debridement of the cornea. In a 1795 letter to Thomas Wedgwood he wrote, "[An] idea is with a sharp knife, to shave or pare off the external part of the opake [sic] cornea, till it becomes transparent, like scraping ivory or horn quite thin, and try if it would become opake again" (pp 95.2–95.3).[75] Parker, in 1894, reported two cases of bullous keratopathy cured by light application of the galvanocautery to the entire corneal surface.[108] Four years later, Ranvier performed the first demonstration of the mechanical sliding of adjacent epithelial cells across a denuded area of human cornea.[112] With better understanding of corneal physiology, the 20th century brought significant advances in the diagnosis and therapy of corneal disease.

Franke, in 1907, was the first to suggest the removal of the corneal epithelium as a therapeutic treatment for corneal basement membrane dystrophy.[42] Over 75 years later, in 1983, Trokel discovered that excimer laser light could be used to reshape and ablate corneal tissue in a more controlled manner.[138] Today, a combination of the techniques proposed over the past two centuries form the cornerstones of the

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ophthalmologist's armamentarium in the diagnosis and treatment of superficial corneal pathology.

2. Techniques

2.1. Blade/Needle

Fundamental to the removal of foreign matter from the cornea, for therapy or diagnosis, is the method adopted to collect the material. A (21–25 G) needle, Beaver blade No. 64 or 57 (Beaver-Visitec International, Waltham, MA) and Bard Parker blade (No. 11 & 15) (BD Medical, Franklin Lakes, NJ) are the most common tools used. Typically, these instruments are reserved for techniques involving the removal of solid foreign objects embedded in the superficial cornea or for collection of infective tissue for microbiological evaluation. Debridement should be done under topical anesthetic at a slit lamp biomicroscope or with the aid of magnifying loupes and a good light source. The sharp edge of the instrument is held tangential to the surface to keep the debridement superficial, thereby reducing the risk of corneal perforation. The Bard Parker blade No. 15 has a shape that allows material to be obtained with relative ease, comes in a sterile single-use package, and is inexpensive. Lim et al describe a technique for corneal foreign body removal that involves bending the tip of a 25 G needle to 90°, increasing the safety and simplicity of debridement.[85]

The use of a blade or needle allows material to be obtained from the leading edge of an ulcer and, by debriding the surface layer, may allow detection of organisms from deeper in the stroma.[73] The Bard Parker blade No. 15 and 21 G needle are useful tools for the collection of infected epithelium for the diagnosis of microbial keratitis (Fig. 1).[54,81,122] Garg feels, however, that a 21 G needle is a poor option for cornea debridement as there is a higher risk of perforation in necrotic corneas.[43] The blade or needle should be scraped over the surface in a series of short, firm strokes from the peripheral margins toward the center of the corneal ulcer to sample both the leading edges and the base of each infiltrated area.[13]

When the Beaver blade is used for epithelial removal in photorefractive keratectomy (PRK), Weiss et al advocate short, rapid, gentle movements of the blade across the cornea to remove epithelium from the periphery toward the center.[1,145] Epithelial debridement prior to PRK must be fast, effective, safe, and able to leave a smooth Bowman layer in order to obtain a successful outcome. A blade has the advantage of complete epithelial removal, but this is highly dependent on surgical skill to complete quickly without damaging Bowman's membrane and exposing the stroma to dehydration.[52] Blades tend to leave microscopic scratches in Bowman's membrane.[1,19,52] Mechanical debridement can also result in ragged edges and a larger than intended ablation diameter.[1]

2.2. Ophthalmic sponge

Sponges have been used in ophthalmic surgery since the early 1980s.[93] The Microsponge (Alcon Laboratories, Fort Worth, TX) consists of methylcellulose in a spear shape of 7 mm base and 17 mm long. Sponges of this material are produced by numerous companies worldwide under various names. Ophthalmic sponges can also be made from polyvinyl acrylate. The sponge is typically used to debride corneal epithelium that is already loose or has been loosened by application of alcohol. Poorly adherent corneal epithelium surrounding a defect or ulcer can be easily removed in this safe and relatively non-invasive technique (Fig. 2).

2.3. Diamond burr

The electric corneal drill, a rotating dental burr, was first introduced for the removal of corneal rust rings in 1936, with subsequent addition of a diamond-dusted tip.[147] Diamond burrs are hand-held, battery-operated instruments with spherical tips of 0.5–5.0 mm diameter. Although specifications vary with manufacturer, rotation speeds average 10,000 rpm, and the diamond-dusted tips are disposable or can be cleaned ultrasonically and autoclaved. Polishing with the diamond burr may be performed with or without continuous irrigation.[107]

Burrs are favored in some centers for the removal of metallic rust rings or scars in the corneal stroma.[85] Diamond burr keratectomy, first used to treat a corneal dystrophy in 1983, is also an effective tool in the management of epithelial

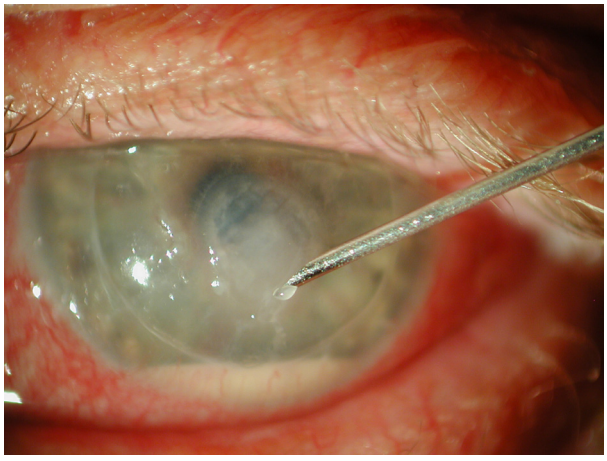

Fig. 1 – Corneal scraping with a 22 G needle for diagnostic sampling of a bacterial keratitis.

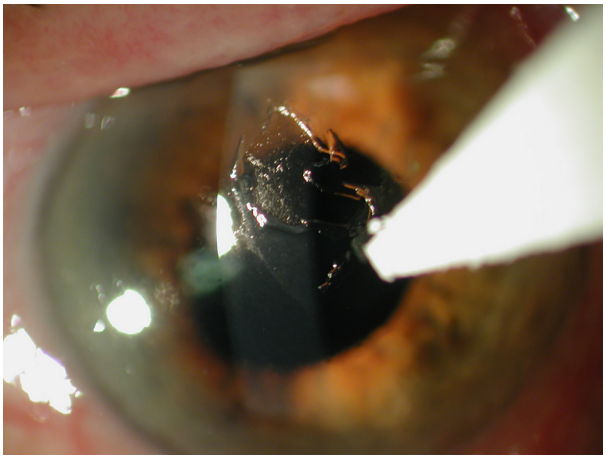

Fig. 2 – Debridement of loose corneal epithelium with a Microsponge for recurrent corneal erosion.

basement membrane dystrophies (EBMDs) and recurrent corneal erosions.[18] Additionally, the diamond burr is used in the operating room after pterygium removal. After instilling topical anesthetic, an eyelid speculum is placed. Loose epithelium is removed with a sponge, and the stromal bed polished with the diamond burr using gentle, uniform circular movements (Fig. 3).[128] A narrow band of epithelium (1–2 mm) should be left at the circumferential limbus to protect the stem cells.

Soong et al highlight the advantages of diamond burr superficial keratectomy as being inexpensive, requiring little skill or expensive equipment, lacking risk of permanent scarring (allowing treatment on the visual axis), with a low chance of perforation and no significant refractive shift.[126] Disadvantages include postoperative pain that may be reduced with a bandage soft contact lens.

2.4. *Kimura spatula*

In 1998, the Kimura platinum spatula was the most commonly used tool for the collection and culturing of microbial keratitis in the United States.[35] Platinum spatulas do not absorb any inoculum, theoretically increasing the yield of corneal cultures. Variations exist, but in general the spatula end is flat and teardrop-shaped with dull edges and a maximum width of 4 mm (Fig. 4). Disadvantages include the possibility of cross-contamination and inconvenience when compared with a disposable instrument.[35] Benson et al suggest that the spatula be used to scrape ulcers for Gram stain and then be reused to inoculate sheep (or horse) blood agar plates.[11] Further scrapes require flaming and cooling of the spatula between each sample.

The spatula is also used to remove corneal epithelium prior to PRK. In this setting, the instrument has the advantage of blunt edges that leave a smooth corneal surface and are unlikely to damage Bowman's membrane.[52] Care must be taken to ensure the blade edges remain regular, as irregularities over time cause uneven debridement. The use of a spatula for de-epithelialization, like the blade, requires a reasonable level of surgical skill to complete quickly and requires epithelial debris to be wiped away with a sponge.

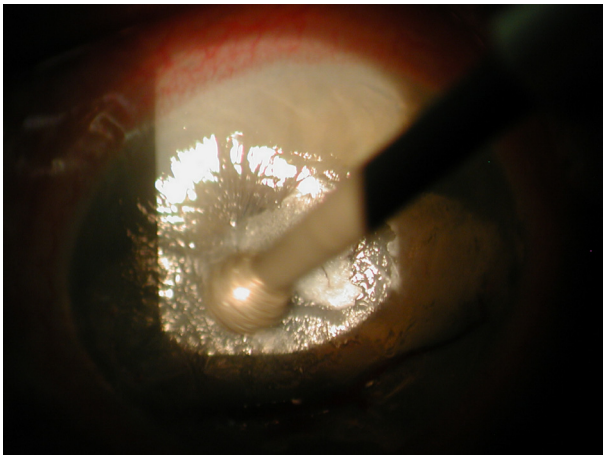

Fig. 3 – Diamond burr superficial keratectomy removal of band keratopathy.

Fig. 4 – Kimura spatula.

2.5. *Amoils brush*

In 1984, Pallikaris et al developed a rotating plastic brush for fast epithelium removal without damage to the basement membrane.[104] The Amoils brush (or Epithelial Scrubber) (Innovative Excimer Solutions Inc., Ontario, Canada)—patented in 1995 as a tool for the clean and effective emulsification of epithelium without damage to Bowman's membrane—is primarily used prior to PRK. This instrument is also used for the treatment of recurrent corneal erosions and has been shown to be simpler, safer, cleaner, and more controlled than methods used in the past.[52,104,123] As the corneal stroma is fibrous, abrasion is limited to only the less robust epithelial cells.

Amoils brush consists of a white plastic handle with a battery-operated motor that rotates a disposable, circular brush. The brush, available in three diameters (6.5 mm, 9.0 mm, and 9.5 mm) with nylon bristles of length 6.0 or 7.0 mm and diameter 80–100 μm, is brought in light contact with the corneal surface (Fig. 5). When applied for 2–5 seconds, the central epithelium is emulsified, leaving a smooth and shiny stromal bed ready for PRK.[123] A longer treatment duration of 30–45 seconds with balanced salt solution irrigation debrides the entire corneal epithelium.[57] This brush effectively removes the epithelium with minimal risk of damage to Bowman's membrane.[52,57,123] Griffith et al demonstrated a strong trend towards more rapid healing of epithelial defects and less postsurgical haze in brushed corneas, when compared with other mechanical or alcohol debridements.[52]

2.6. *Epikeratome*

The Epikeratome, designed for epithelial removal prior to Epipolis Laser In-Situ Keratomileusis (Epi-LASIK), eliminates the need for hand-held mechanical or chemical debridement. The Epikeratome is a modified microkeratome with a customized block that mechanically separates the epithelium from Bowman's layer as an intact sheet of viable tissue (Fig. 6). The instrument operates under suction with forward

Fig. 5 – Removal of corneal epithelium with an Amoils brush prior to phototherapeutic keratectomy.

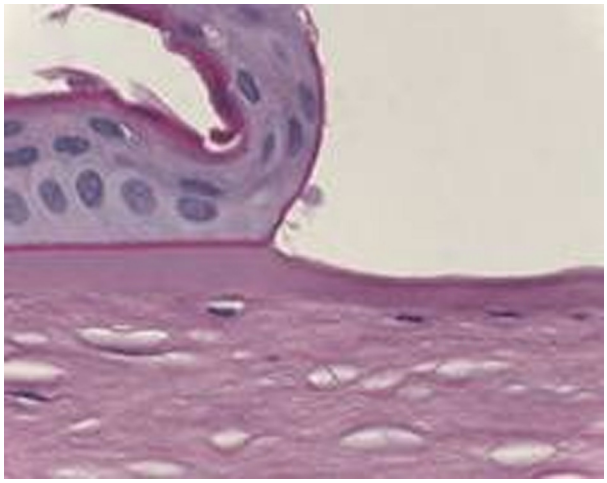

Fig. 6 – Histological section showing dissection plane between the epithelial basement membrane and the underlying Bowman's membrane following epikeratome pass (hematoxylin and eosin stain, 400× original magnification).

oscillation of a blunt polymethylmethacrylate separator at 12,000 rpm parallel to the horizontal corneal plane.[69,104] This leaves a smooth, uniform bed for refractive ablation. The 9 mm epithelial flap can then be discarded or repositioned according to the surgeon's preference. There are disposable tips or cassettes that attach to a reusable stainless steel handle.

The instrument, as described by the patent holders, Pallikaris et al, leaves an intact basement membrane, thus enhancing healing of the corneal epithelium.[104,105] In this way, this technique is less invasive to epithelial structure than chemical debridement.[105] There are, however, costs associated with the initial keratome set-up, as well as ongoing disposables. Adverse effects of epikeratome use include postoperative pain, delayed visual rehabilitation, incomplete epithelial flaps, and the risk of haze.[74,103,137]

A more recent development is the Epi-Clear (ORCA, Upper Gallilee, Israel), a multi-blade polymer device that performs surface epithelium removal in one 8-second sweep. There are no published trials utilizing this instrument; the manufacturer, however, states that it can be used for refractive surgery, in keratoconus, or on recurrent corneal erosions. There are adjustable suction rings to control epithelial flap diameter.

2.7. *Excimer laser*

Excimer lasers, developed to etch highly precise patterns into plastic, are a mixture of argon and fluorine gas inside a tube, emitting light of wavelength 193 nm.[121] Trokel was the first to realize that ultraviolet light of this wavelength allows precise removal of corneal tissue through a photochemical laser–tissue interaction.[138] He predicted in 1983 that this new technique had implications for a variety of corneal surgical procedures, from corneal incisions to refractive keratoplasty.[138] The excimer laser proved useful for photorefractive and phototherapeutic corneal modification.[39]

Ultraviolet light with high energy is absorbed immediately by the corneal surface. The mechanism of interaction between the photons and biologic molecules is unknown, but it may be that the ultraviolet light breaks chemical bonds directly. In this way, part of the superficial tissue is ablated. One 20-nanosecond pulse of light typically ablates 0.1–0.5 μm of tissue. Laser delivery patterns include broad beam, scanning slit, and flying spot. Broad beam lasers deliver a beam that starts small and expands during delivery. These lasers are associated with a shorter operating time; the energy consistency is difficult to control, however, and central islands may occur. Scanning slit and flying spot patterns provide a smoother ablation concentrating the treatment to the central cornea. These lasers can produce aspheric and large diameter ablations even when the cornea is aspheric or irregular.

The key feature of the corneal surface immediately after ablation with the excimer laser is its smooth contour, superior to that obtained with the highest quality microkeratomes. This smoothness, however, may be quickly degraded by intraoperative or postoperative dehydration. The laser itself ablates tissue and does not smooth the surface on its own. If the treatment surface is irregular, the final surface will mirror this. This can be prevented by the use of a masking agent, such as methylcellulose, applied frequently during the procedure.[59]

In order to expose Bowman's layer and the underlying stroma, the corneal epithelium must be removed prior to treatment with the excimer laser. This can be done mechanically, chemically, or with the laser itself (termed photoablative de-epithelialization). When the laser is in phototherapeutic keratectomy mode and the epithelium is ablated, it must be removed with a mechanical instrument; this technique is called "laser-scrape".[1] This process has limited precision, as the excimer laser must be programmed for a predetermined epithelial thickness.[123] Advantages of laser epithelial removal, however, include a short surgical time, less technical demand, and minimal damage to surrounding tissues.[48,83]

Potential side effects of excimer laser use can be subdivided into thermal, mechanical, or actinic.[121] Thermal damage to neighboring tissue may occur as the result of heat dissipation from a treated area to a non-irradiated portion of tissue. This rare side effect may result in a self-resolving, visible pseudomembrane at the treatment border. Epithelial debridement and shock waves during ablation may cause mechanical damage to the deeper layers of the cornea. Actinic damage or mutagenic potential of 193 nm wavelength light was not insignificant in longitudinal studies of PRK.[121] Longer-term complications also include refractive changes such as hyperopic shift from corneal flattening, tear deficiency, recurrent erosions, subepithelial opacities, and decreased corneal sensitivity.[59]

3. Diagnostic indications

3.1. *Keratitis*

Management of acute microbial keratitis requires the procurement of corneal material from the ulcer for preparation

of smears and cultures prior to treatment. The American Academy of Ophthalmology publishes standard guidelines for the management of infectious keratitis that are reviewed annually.[106] Corneal debridement, swabs, and/or corneal biopsy provide the specimens required for direct microscopic detection of the causative organism, for culture, and to identify the sensitivity to antibiotic agents.[79,84,90,91]

The cornea is debrided under magnification and topical anesthesia. An aseptic technique is employed for handling of specimens. Care is taken to avoid contact with the eyelids during debridement. The specimen can be collected with a Bard Parker No. 15 blade (Fig. 7), disposable 21–25 G needle (Fig. 1),[122] calcium alginate swab,[11,12,131] Kimura spatula,[12,67,131] or similar.[54] The base and leading edge of the ulcer should be scraped gently but firmly from the periphery to the center. The debridement is repeated several times using a fresh instrument, or by re-flaming and cooling the spatula, to obtain samples that are immediately transferred onto collection media (Fig. 8).[81]

Benson and Lanier compared the platinum spatula and calcium alginate swab moistened with trypticase soy broth.[11] They found greater colony growth from the moistened swab, perhaps due to better absorption of the organisms onto the swab and their release onto the solid agar media. The platinum spatula, owing to its poor absorptive properties, showed better preservation of cells but less growth on agar. Benson and Lanier suggest the use of a Kimura spatula to scrape the ulcer for a Gram or additional stains.[12] The Kimura spatula can then be used to rescrape the ulcer and directly inoculate plates, and a calcium alginate swab is used to streak the same plates for increased potential organism yield.[11] The calcium alginate swab should be avoided, and a dacron swab used instead, if PCR tests may be required, as these swabs may inhibit growth of certain infectious entities including herpes virus. Due to the high colony growth associated with the use of the calcium alginate swab, there is an increased risk of collection and culture of commensal organisms.[63]

In a retrospective study of 1,092 eyes with early or advanced keratitis, Sharma et al found that Gram stain of corneal debridements in early keratitis have a low sensitivity, specificity, and predictive value (36.0%, 84.9%, and 70.3% respectively).[122] They found a higher positive predictive value (82.7%) in the 841 eyes with advanced keratitis and suggest that it would be reasonable to initiate specific therapy for organisms seen in the Gram stain in these eyes.[122] Gram stain has a much higher sensitivity in the detection of fungi (89.8%) and *Acanthamoeba* (73.3%), when compared with bacteria (56.6%).[49] A study of 3,298 eyes with infective keratitis found a Gram stain sensitivity of 100%,[13] much higher than previous reports.[8,49,86,122] Variations of conventional Gram stain, such as fluorescent Gram stain, are of limited value in the diagnosis of microbial keratitis.[119]

There continues to be a discrepancy between formal recommendations and community practice in the management of corneal ulcers. This nonconformity with guidelines for the management of infectious keratitis may relate to high cost, poor reimbursement, insufficient time for microbiological tests, logistic barriers, or practitioner skepticism about published recommendations.[43,87] The high success rate with current antibiotic therapy may also contribute to the low rate of tissue sampling for diagnosis by ophthalmologists.[118] McDonnell et al surveyed ophthalmologists in California and found that 49% of corneal ulcers were treated without obtaining any cultures.[88] In the event that resistant organisms are encountered and antibiotic therapy must be changed, it can be difficult to make a therapeutic decision without the benefit of microbiology.[92] Dahlgren et al surveyed 89 ophthalmologists for their clinical diagnostic accuracy compared with culture confirmed corneal infection. The study found ophthalmologists had a 92% sensitivity (95% confidence interval [CI], 83–97%), 37% specificity (95% CI, 20–56%) and 78% positive predictive value (95% CI, 68–86%) and were able to classify ulcers as infective or noninfective in 76% (95% CI, 67–84%) of eyes. A study published in 2012 found that corneal experts were better than chance at distinguishing bacterial from fungal ulcers, but were accurate only 60–70% of the time and were less successful at identifying Gram stain results, genus, or species.[23] This indicates ophthalmologists should communicate their preliminary diagnostic suspicion to

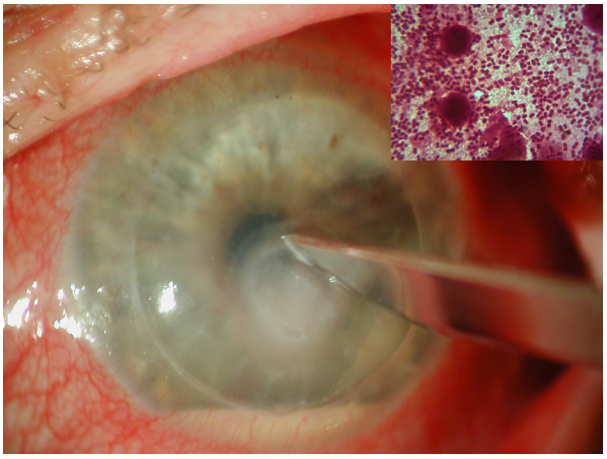

Fig. 7 – Corneal scraping with a Bard Parker no. 15 blade for diagnostic sampling of a bacterial keratitis. Inset shows Gram negative coccobacilli identified as a *Moraxella* species (Gram stain, 400× original magnification).

Fig. 8 – Corneal scraping kit showing agar plates, broths, viral transport medium, and disposable needles.

microbiologists. Clinical examination, however, cannot be used as the only basis for treatment decisions in microbial keratitis.[13,22]

Corneal biopsy is the definitive investigation in progressive microbial keratitis.[6] Although there is the risk of irregular astigmatism induction and localized corneal thinning, unresolved progressive keratitis has a far poorer visual prognosis. Corneal biopsy is an important diagnostic tool that should be considered in patients responding poorly to the administered antibiotic, particularly if fungi or *Acanthamoeba* are suspected.[2,54]

3.2. *Neoplastic*

Von Graefe first described squamous neoplasms of the ocular surface in 1860.[10] Both invasive and noninvasive forms occur.[10,82] In 1995 Lee and Hirst proposed the term ocular surface squamous neoplasia (OSSN) to encompass the entire spectrum of dysplastic and carcinomatous lesions of the ocular surface.[82] The accurate diagnosis of squamous lesions of the cornea and conjunctiva is important because of their potential for ocular and even systemic morbidity and mortality.[10] The extent and severity of these uncommon lesions should be carefully evaluated early in the course of the disease. As the diagnosis cannot definitively be made on clinical appearance alone, tissue is needed to identify malignancy.[133] Both exfoliative and impression cytology allow staging and diagnosis of ocular surface tumors.[124,127,140] Preoperative information regarding the nature of the lesion, obtained by a noninvasive technique, is an important guide to planning therapy.[36]

3.2.1. *Exfoliative cytology*

In 1954, Larmande and Timsit used a sterile platinum spatula to obtain a specimen that they stained with a Papanicolaou technique and found that positive cytologies correlated with subsequent histological examinations.[80] The exfoliative method of obtaining diagnostic conjunctival cytological material debrides the conjunctival surface with a spatula, cotton swab, or cytology brush.[46,53,150] Malignant cells of mucosal surfaces are particularly well-suited for exfoliative cytology because of their poor intercellular adherence and tendency to desquamate.[10] Spinak and Friedman presented two cases in 1977 to demonstrate that exfoliative cytology with a blade was a rapid and useful technique for the study of suspicious lesions of the bulbar and palpebral conjunctiva.[127] Gelender and Forster then used a heat sterilized platinum spatula to scrape suspicious lesions in 41 eyes and found that Papanicolaou staining correctly predicted neoplasia in 13 of 14 cases.[46] Twenty-five of their 27 benign lesions were accurately classified using cytology.

Tsubota et al, the first to report the use of a brush for the collection of surface cells and conjunctival cytology,[142] suggested that the material be collected, then spread on glass slides and fixed with 100% methyl alcohol for 30 minutes. They suggest that a whole layer of cells, including deep basal, can be collected with less intervention than debridement.[141] Further, cells appear less overlapped, allowing better morphologic identification. Yagmur et al prospectively studied the efficacy of brush cytology as compared to impression cytology.[150] They debrided the ocular surface with several gentle rotations of the brush under slit lamp observation. The material was smeared onto a slide by rotations of the brush and fixed with 95% ethanol prior to Papanicolaou staining. Clinical and cytological concordance was 97% in the brush technique group. They concluded that brush cytology is superior to impression cytology for obtaining an adequate cellular population and in the morphological quality of the cells.[150] Ersoz et al found that, in addition to preserving cell morphology, brush cytology smears were easier and faster to prepare.[36]

Lee and Hirst commented on the relative disadvantages of exfoliative cytology, including patient discomfort and the need for an experienced pathologist to interpret the specimens reliably.[82] Further, this method of cytology does not localize the sampled lesion, nor does it indicate the degree of tumor invasion.[46,82] Basti and Macsai comment that cellular overlap in exfoliated samples may obscure some of the cellular details, which may further be altered by drying artifacts.[10]

3.2.2. *Impression cytology*

Impression cytology removes cells from the superficial layers of the ocular surface by applying a collecting device, to which the cells adhere and from which they can be removed and processed for further analysis.[133] Impression cytology using a piece of cellulose acetate filter paper was first adopted by Egbert et al as a simple procedure for conjunctival biopsy in 1977.[32] This method was modified by Tseng et al in 1985 to capture more accurately conjunctival changes in squamous metaplasia.[140] Pieces of cellulose acetate filter paper cut into a pointed tip were applied to the bulbar conjunctiva for 2–3 seconds. The filter paper was then placed in fixative solution, and underwent a complex staining protocol. They also used a modified Papanicolaou stain and were able to describe six different stages of squamous metaplasia. Nolan et al used this method and found a high predictability rate of 77% (55 of 71 eyes) for microinvasive carcinoma.[98] Nolan et al and Tseng et al conclude that the diagnosis of squamous metaplasia is more accurately made by impression cytology than by any other means.[98,140] This technique, although effective, has been described as cumbersome and time-consuming, therefore perhaps inappropriate for ophthalmology outpatient settings.[10,136]

The Biopore membrane (Millipore Corp, Billerica, MA), first described by Thiel et al,[134] was applied to diagnosis of OSSN by Tole et al in 2001.[136] The Biopore membrane disc is 8 mm in diameter and attached to a small plastic tube. The membrane disc is pressed against the area to be sampled for 10–20 seconds, then immediately transferred to a container of 95% alcohol. The specimen is stained with hematoxylin and eosin. Tole et al found a high correlation rate of 80% (in 25 eyes) for predicting subsequent histological findings using the Biopore membrane.[136] This technique is easy and rapid to use in clinical settings, with 96% of first-time user ophthalmologists able to obtain adequate samples.[136] A limitation of any technique of impression cytology is the required expertise of the pathologist in assessment of the unique cytology of the ocular surface.[98,136]

4. Therapeutic indications

4.1. *Recurrent corneal erosion*

Recurrent corneal erosion (RCE) or recurrent erosion syndrome is a disorder of the epithelial basement membrane frequently associated with a history of superficial corneal injury or evidence of EBMD (epithelial basement membrane dystrophy—also termed Cogan dystrophy, map-dot-fingerprint dystrophy, or microcystic epithelial dystrophy).[24,71] In the majority of patients, RCE is characterized by repeated episodes of pain, difficulty opening the eyes, blurred vision, watering, and photophobia secondary to poor epithelial adhesion. This clinical entity was first described by Hansen in 1872 and was termed 'intermittent neuralgic vascular keratitis'.[55] The number and variety of treatments employed over the ensuing 100 years emphasizes the recalcitrant nature of the disorder.

The basic goal of treatment in RCE is to improve the adhesion of the epithelium to the underlying basement membrane complex. A variety of adhesion complex defects have been observed in RCE, including reduplication of basement membrane, loculation of connective tissues, and absence of basement membrane and hemidesmosomes.[9,30,111] The majority of patients will respond to conventional forms of therapy, including patching, cycloplegia, and topical antibiotic ointment. Medical treatment lubricates the ocular surface and maximizes the health of the tear film. Conservative treatment in the form of topical lubrication, hypertonic agents, and soft bandage contact lenses are initial therapeutic choices to prevent recurrences.[146] Approximately 5% of patients fail to achieve resolution of the acute episode with these measures, and 60% continue to have persistent symptoms.[60,116]

When RCE recurs despite medical therapy, surgical intervention is usually necessary to stimulate new and stronger epithelial adhesion complexes.[57] Such strategies include removal of the loose epithelium by mechanical debridement, superficial keratectomy, or excimer laser phototherapeutic keratectomy (PTK).[144] The formation of subepithelial scar tissue with Nd:YAG (neodymium:yttrium-aluminium-garnet) laser treatment or needle anterior stromal puncture also promotes epithelial stability.[45,120,144] The choice of surgical approach is determined by the frequency and severity of erosions, the presence of concomitant dystrophies, the etiology and location of erosions, and the patient's preference.

4.1.1. *Debridement and superficial keratectomy*

Historically, debridement and then superficial keratectomy were the first surgical approaches to the treatment of RCE, and these procedures remain in use today. Franke, in 1906, treated recurrent corneal erosion by debriding the epithelium and applying chlorinated water.[42] Debridement, useful for the removal of loosely adherent epithelium, promotes healing from the healthy edge.[111] The poorly adhered epithelium may be removed with a sterile sponge (Fig. 9), Kimura spatula, or a Bard-Parker blade No. 15. In a retrospective series, Reidy et al treated 11 patients with this method, with a recurrence rate of 18%.[116] Rubinfeld found a statistically significant improvement in best-corrected visual acuity after simple mechanical debridement, and a 5-year probability of recurrence of 44.7%. Itty et al studied 74 eyes and found improvements in mean and median visual acuity post debridement, and concluded that simple mechanical debridement of corneal epithelium and redundant basement membrane is an effective method of treating EBMD.[62] Although debridement of loose epithelium hastens resolution of the acute episode, there is no prospective evidence that this reduces the recurrences of RCE.[16,38,60,111] Ramamurthi et al suggest that this treatment should only be used when the epithelium is freely mobile on the underlying stroma and discourage debridement of stromal tissue.[111]

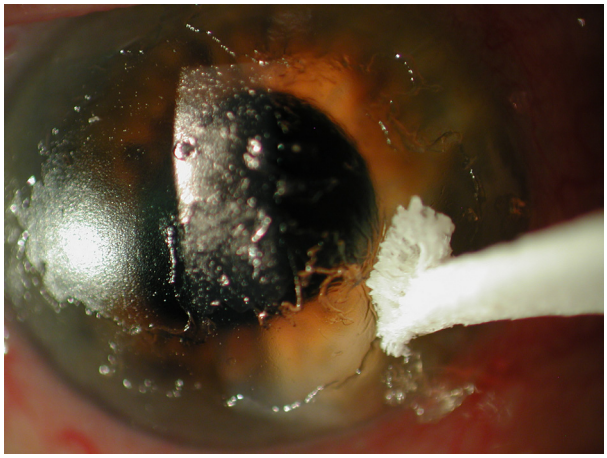

Fig. 9 – Extensive debridement of loose corneal epithelium to the limbal zone with a Microsponge for recurrent corneal erosion.

Superficial keratectomy for EBMD, as described by Buxton and Fox in 1983, establishes a superficial plane of dissection in the superior paralimbal region with a razor blade fragment or diamond knife.[17] Dystrophic tissue, consisting of epithelium and basement membrane, peels off in a continuous sheet, leaving Bowman's layer undisturbed. The complete removal of epithelium and basement membrane allows for the regeneration of corneal epithelium and conjunctival epithelial cells.[17] Buxton and Constad reported 30 patients, of which 27 had diamond burr paralimbal polishing post superficial keratectomy.[18] Of the three patients treated with debridement alone, two had recurrent symptoms. They identified the optimum candidate for this procedure as having multiple erosions in different areas of the cornea, no history of trauma, severe EBMD resulting in poor vision, and large areas of loosely adherent epithelium.

4.1.2. *Diamond burr superficial keratectomy*

Diamond burr keratectomy is a convenient method of polishing Bowman's membrane that can be carried out in the examining room under slit lamp biomicroscopy (Fig. 10). The loose epithelium is first removed with a microsponge or blunt spatula. Polishing Bowman's membrane with the diamond burr should take 5 to 10 seconds,[107] although some advocate up to 30 seconds.[148] After a smooth, uniform surface is obtained, a cycloplegic agent and antibiotic ointment should be

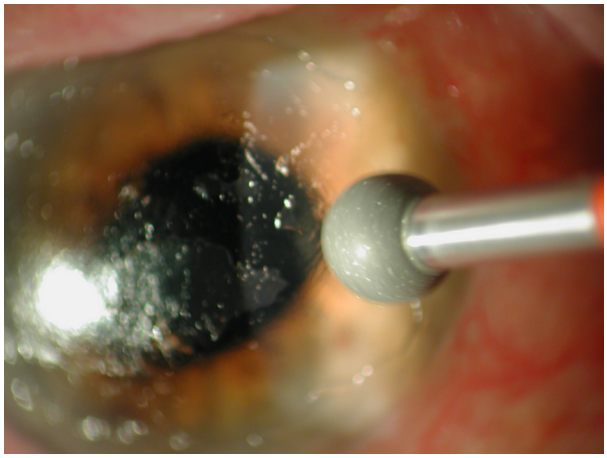

Fig. 10 – Diamond burr superficial keratectomy of the Bowman's membrane following epithelial debridement for recurrent corneal erosion.

applied prior to patching.[107,128,148] This technique is generally safe with a low rate of recurrence.[126,128,143,148] Soong et al retrospectively collected 54 eyes treated with diamond burr keratectomy and found it to be a good alternative surgical therapy for the simple and safe removal of epithelium without the risk of scar formation.[126]

In a study conducted at the Wills Eye Hospital, 13 eyes were treated with epithelial debridement of the central epithelium, followed by diamond-dusted burr polishing, which yielded a decreased incidence of recurrent erosions over debridement alone.[143] Best-corrected visual acuity improved by almost 50% (0.40 to 0.88 logMAR) at the last follow-up (median, 21.8 months).[143] Sridhar et al retrospectively compared diamond burr and PTK treatment of RCE in 42 eyes with EBMD.[128] They found recurrence of erosions in 11.1% and 26.7% of the diamond burr and PTK treated eyes, respectively. There was no significant difference in postoperative haze or visual acuity between the two groups, and both therapies were deemed to be effective. They conclude that diamond burr treatment has advantages over PTK, being simpler, with a tendency toward lesser incidence of haze and recurrence.[128] In contrast, Reidy et al observed recurrence in one of four patients treated with diamond burr keratectomy.[116]

Wong et al carried out a double-masked randomized control trial to compare diamond burr polishing with epithelial debridement alone.[148] They felt that the diamond burr is effective because of the smooth surface it leaves upon which new epithelium can grow.[148] Additionally, reactive fibrosis and expression of extracellular matrix proteins may be stimulated, thereby allowing scarring and stronger epithelial adhesion to underlying stroma. They found that diamond burr keratectomy results in a lower recurrence rate of RCE compared with debridement alone and confirmed previous observations that diamond burr polishing results in a significant decrease in mean magnitude of astigmatism.[143,148] This is the only randomized-control trial of RCE treatments and is particularly limited by a short follow-up period (6 months).

Hodkin and Jackson were the first to suggest the use of the Amoils brush was a safe and effective tool for treating recalcitrant RCE.[57] In PRK, the Amoils brush is applied to the epithelium for 2 to 5 seconds. Hodkin and Jackson applied the 6.5 mm brush for 30 to 45 seconds to ensure complete polishing of Bowman's membrane.[57] In this retrospective case series of 26 eyes, resolution of RCE symptoms was achieved in 88% during the follow-up period (mean, 21.2 months; by telephone survey). The 12% failure rate was thought to be the result of incomplete debridement of the far peripheral cornea. Advantages of this procedure are the simplicity, cost effectiveness, and safety in the preservation of Bowman's layer, although patients had more postoperative pain compared with other procedures.[57,104]

4.1.3. *Anterior stromal puncture*

McLean et al described an alternative management of RCE that they termed 'anterior stromal puncture'.[89] This technique was based on the clinical observation that recurrent erosions generally occurred either spontaneously or after superficial trauma, yet were rarely seen after embedded corneal foreign bodies or superficial stromal. They hypothesized that the crucial difference was in the preservation of Bowman's membrane.[89] With this in mind, they used a 20 G disposable hypodermic needle to make multiple punctures through loosened epithelium and Bowman's membrane into the anterior half of the stroma. In general, 15 to 25 punctures were made over the treatment area, spaced 0.5–1.0 mm apart. They proposed that this procedure resulted in improved adhesion of the epithelium to the underlying stroma, which was later confirmed by Katsev et al by electron microscopy.[70] Needles of 23–30 G were compared, and the depth of penetration with smaller gauge needles was less predictable. An insertion depth of 0.1 mm was sufficient to cause fibrocytic reaction.[70]

The safety of anterior stromal puncture is shadowed by the risk of perforation and scarring, which is likely to affect vision if there are multifocal scars or irregular topographic changes affecting the visual axis. If a 27–30 G needle is used under an operating microscope, the technique is considered safe and effective.[24] Anterior stromal puncture also offers the advantages of a low risk of refractive power change and less discomfort when compared to other treatment modalities for RCE.[24]

Geggel and Maza used the Nd:YAG laser to disrupt anterior stroma, as an alternative to needles, and found that the laser produced reproducible shallow incision depths with only minimal stromal scarring.[45] They advocate focal debridement of loose epithelium prior to treatment and energy levels between 1.5 and 2.5 mJ as appropriate for human corneas. Katz et al modified Geggel's technique so that debridement was not necessary and termed the technique 'Nd:YAG laser photo-induced adhesion'.[72] They treated eight patients in this way and reported no recurrences over a mean 21.2 months follow-up. They also concluded, through electron microscopy, that a break in Bowman's layer was not required for the YAG laser to be effective and was perhaps undesirable.[72] Katz advocates the use of the lowest energy setting of the YAG laser (0.4–0.5 mJ) in order to prevent Bowman's membrane disruption and subsequent scarring.[71]

Tsai et al report the largest series of eyes to date (n = 33) treated with Nd:YAG anterior stromal puncture for RCE.[139] They found 49% of eyes were completely symptom-free postoperatively, and 36% had subjectively mild symptoms. The remaining 15% of eyes with recurrence of corneal epithelial defects had a statistically and clinically significant decreased frequency of episodes (12.2 to 1.9 episodes/year).[139] They make the point that as well as having the advantage of a minute and uniform wound, the Nd:YAG laser energy pulse is invisible and less frightening for the patient than treatment with a needle.

4.1.4. *Phototherapeutic keratectomy*

The use of excimer lasers for PRK suggested a role for photoablation in the treatment of superficial corneal pathologies.[24] Despite the iatrogenic production of a corneal defect as part of the PRK procedure, there was no long-term epithelial instability in these patients.[24,39] Dausch and Schroder reported the first series of patients successfully treated for RCE with the excimer laser in 1990.[26] The advantages of these lasers include the ability to remove corneal tissue with extreme precision and minimal adjacent tissue damage and the large beam cross sections that allow simultaneous treatment of wide areas.[100] PTK was approved in the United States in 1995 for the laser treatment of superficial corneal dystrophies, epithelial basement membrane dystrophies, and corneal scars or opacities.[114] Interestingly, RCE was not included as there was insufficient evidence that PTK was superior to other therapies.

Prior to PTK, the epithelium is usually removed mechanically by debridement with a spatula or blade to avoid the projection of surface irregularities. The ablation method commonly used involves the 193 nm laser light emission, with a repetition rate up to 50 Hz and diameter 6.5 mm. No more than four shots should be performed on one area in order to preserve Bowman's layer. With a superficial ablation of 5–6 μm, there is minimal postoperative refractive change.[64,102,113] Rapuano also recommends treatment of the entire visual axis to decrease the risk of visually significant irregular astigmatism.[114,115] Using this technique, Morad et al reported a recurrence-free rate of 83% (mean follow-up, 40 months),[96] similar to that reported by Dausch et al of 75%[25] and O'Brart et al of 74% (mean follow-up, 11 months).[100] Both Forster et al and Algawi et al reported that none of their PTK treated patients experienced recurrence of corneal erosions.[3,7,41] Ohman and Fagerholm found that greater than 90% of excimer laser treated eyes were symptom-free for 12 months postoperatively, compared with 50% with manual epithelial removal alone.[102] Jain and Austin achieved best results in eyes with post-traumatic erosions (80% asymptomatic post PTK) compared to idiopathic corneal erosions (53.8% asymptomatic post PTK).[64] Corneal irregularity after treatment is a common complication if a masking agent is not applied. Masking agents, such as methylcellulose or sodium hyaluronate, should therefore be used.[5]

A recent large cross-sectional study of PTK for EBMD found symptomatic recurrence in 13% of eyes and morphologic recurrence in 40%.[47] Mean follow-up was 43 months and no eyes required retreatment during this time, with 98% showing unchanged or improved visual acuity. Morphologic recurrences were associated with laser epithelial removal.[47] Most long-term studies of corneal erosion recurrence after PTK have found that the majority of recurrences occur within the first year.[9,20,28]

O'Brart et al found minimal complications after PTK and no evidence of disturbance in corneal transparency associated with the photoablative treatment persisting 6 months after surgery.[100] This maintenance of corneal transparency and the precision with which corneal tissue can be removed has seen superior patient and surgeon satisfaction when compared to stromal puncture.[44,100,114] Although statistically significant refractive change is not reported with this procedure, there is a trend towards hyperopia documented.[20,44,64,114,152] Kremer and Blumenthal combined PRK and PTK to overcome refractive concerns.[77] The other disadvantage of PTK is postoperative pain. Ardjomand et al found that a modified PTK technique where a hinged epithelial flap is placed back on the stroma post treatment reduced postsurgical pain in their nine patients.[7] Their procedure, however, results in the reapplication of the pathological epithelium and basement membrane, which appears counterintuitive.

Overall, PTK is a safe and effective treatment for the management of RCE and EBMD, although it is limited by refractive changes and postoperative pain. Its high cost and lack of widespread availability has restricted its use in general ophthalmic practice.

4.1.5. *Alcohol delamination*

Alcohol delamination of the corneal epithelium is known to leave a smooth surface and is used in some centers prior to laser epithelial keratomileusis (LASEK).[1] Alcohol delamination prior to PRK is reproducibly quick, easy to perform, gentle on Bowman's layer, and causes minimal inflammation and keratocyte loss.[1,38] Dua et al first reported this technique for the treatment of RCE.[30] By cleaving and removing the abnormal basement membrane and leaving behind a very smooth surface, alcohol delamination enables firmer adhesion of new epithelial cells. In a prospective study, Singh et al found that up to 83% of patients were symptom-free after intervention and 91–100% of patients had decreased symptoms of pain post treatment.[125] Like Dua et al,[30] they used a 20% alcohol solution placed in a 4 or 5 mm optical zone marker for 40 seconds. The alcohol was removed with a Microsponge and the epithelial sheet was peeled away with a spatula. Alcohol delamination is a promising treatment for RCE, with a safety and efficacy comparable to PTK, but with the advantage of a wider availability and significantly lower cost.

Variations of these techniques may be applied to other corneal disorders, including bullous keratopathy, foreign bodies, and corneal opacities and dystrophies, but this discussion lies outside of the scope of this review.

4.2. *Band keratopathy*

Calcific band keratopathy, first described by Dixon in 1848, is a chronic degenerative condition characterized by the deposition of grayish to whitish opacities in the superficial layers of the cornea (Fig. 11).[29] This condition is associated with systemic conditions causing hypercalcemia such as

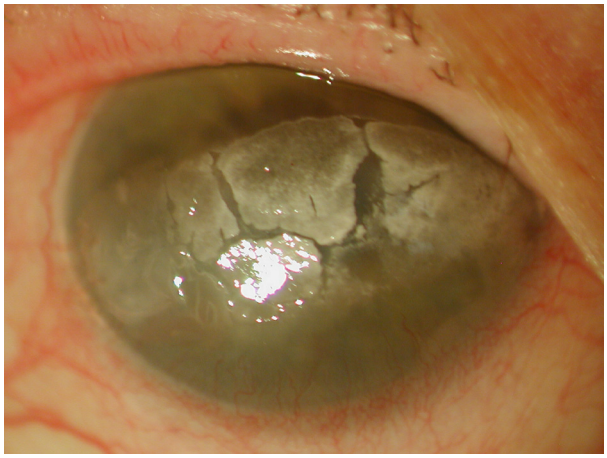

Fig. 11 – Band keratopathy.

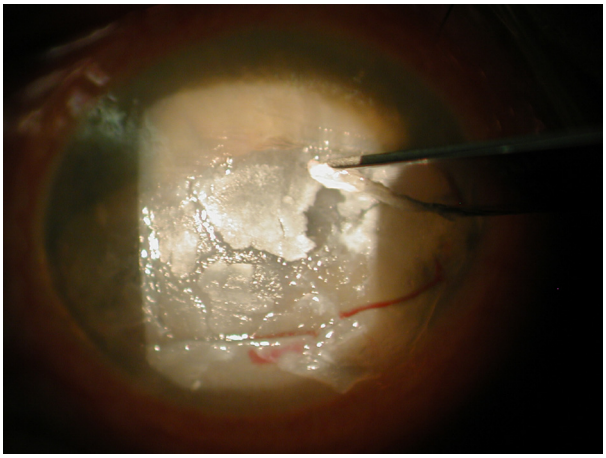

Fig. 12 – Superficial debridement of band keratopathy plaque with a Bard Parker no. 15 blade.

sarcoidosis or chronic renal failure, or with chronic ocular inflammation such as in chronic uveitis or long-standing interstitial keratitis.[61] In general, the calcium deposits in Bowman's layer and in the superficial lamellae of the stroma.[66] The calcium haze is often separated from the limbus by a clear zone and may develop a "Swiss cheese" appearance with scattered holes inside the band, thought to represent the penetration of Bowman's layer by corneal nerves.[66,97,101]

The aim of surgical treatment is to remove the opaque calcium deposits and to restore the smooth corneal surface. With treatment, an improvement in both visual acuity and glare is expected in the majority of patients with smooth calcific bands; however, procedures are performed to improve ocular comfort in eyes with poor visual potential.[97,130] Treatment may also be indicated prior to intraocular surgery or for easier examination and treatment or follow-up of patients with posterior segment disease.[130] Chelating agents, for example, ethylenediaminetetra-acetic acid (EDTA) and superficial keratectomy, were considered standard treatment until the early 1990s.[99] In recent years other surgical methods such as PTK,[99,130] superficial lamellar keratectomy,[78] and combined techniques with amniotic membrane transplant,[37,61] have developed.

4.2.1. *Superficial keratectomy*

The ease of surgery and minimal cost of mechanical removal make superficial keratectomy the mainstay of band keratopathy treatment in the developing world.[66] Where the calcium plaque is thick, it can be removed with forceps, or a blade (Fig. 12). In 1975, Wood described this technique as being "much like sharpening a razor on a leather strop (p 550)."[149] This often, however, results in an irregular corneal surface, and the depth of treatment is also hard to control.[99] There are few recent reports of superficial keratectomy alone for the treatment of band keratopathy, given the less invasive options available today.

Bokosky et al used a diamond burr for removal of calcific band keratopathy (Figs. 3 and 13).[14] They found that this was an effective and simple method of removing resistant deposits from the cornea without causing scarring. Further use of this technique has not yet been described.

4.2.2. *Chelating agents*

Chelating agents are compounds that, by forming soluble complexes with specific metals or compounds, extract them from the milieu in which they occur.[15] The favored solution for the chelation of calcium in band keratopathy is disodium EDTA. The goal of this therapy is to remove the calcium opacities and restore a smooth ocular surface. Initial reports in the 1950s suggested the use of 15-minute application of 0.01–0.05 M solution after epithelial debridement.[15,51] There were few reports of EDTA chelation in the literature again until Najjar et al published a retrospective case series of 65 eyes in 2004.[97] They used a 3.75% dilution of disodium EDTA applied to an anesthetized cornea for up to 45 minutes, depending on the density of calcification. The mean time to epithelial healing was 8 days. Over a mean follow-up period of 36.6 months (standard deviation, 68.9 months), they found 90% of patients had partial or complete symptomatic relief. There was a recurrence rate of 18%; mean time to recurrence, however, was 18 years.

Kwon et al treated two cases of band keratopathy with superficial lamellar keratectomy, EDTA chelation, and

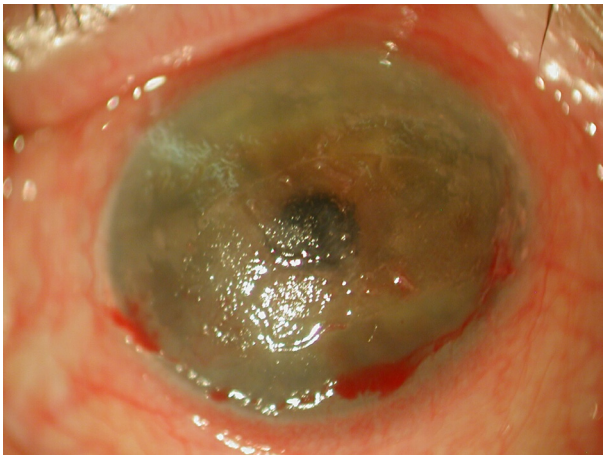

Fig. 13 – Post-corneal debridement with blade and diamond burr following removal of band keratopathy.

amniotic membrane transplantation.[78] They reported minimal inflammation and swift return to corneal clarity with no recurrence over 14 months. They advocate that this is a safe and effective combination to remove calcified lesions and restore a stable ocular surface. Their results were corroborated by Im et al, who combined PTK, EDTA, and amniotic membrane transplant.[61] They found that they were able to treat thicker and deeper plaques successfully. Youssef et al removed an epithelial flap and applied 0.05 M EDTA solution to the cornea for 30–60 seconds with a LASEK solution reservoir.[151] They then repositioned the epithelium to act as a bandage contact lens. This technique has reduced surgical time and mechanical trauma to the cornea as a result of the use of the surgical well.

4.2.3. *Phototherapeutic keratectomy*

The indiscriminate ablative action of PTK means that all bands, independent of biochemical makeup or texture, can be treated.[130] The first large retrospective case series examining the use of excimer laser PTK for band keratopathy was published by O'Brart et al in 1993.[99] They reported 122 eyes treated with a 4.0–5.0 mm ablation zone without epithelial debridement. In the case of rougher keratopathy, they mechanically removed large calcified plaques. They found that differential fluorescence between the band and the stroma gave a precise end point for laser exposure, and less than 300 pulses were usually required per eye. In routine practice, however, some suggest graded ablation with intraoperative assessment of corneal clarity.[66] Postoperatively, O'Brart et al reported 90% of patients with smooth band keratopathy demonstrated improvement of visual acuity and glare.[99] There were nine cases of recurrence, five of which occurred in patients who developed band keratopathy secondary to silicone oil. Stewart et al used a similar technique, but included epithelial debridement prior to PTK in all cases.[130] Their study of 45 eyes found no significant recurrences up to 2 years following PTK. They hypothesize that the increased tear film stability post PTK may be the result of improved mucin production by a healthier epithelium.

Limitations of PTK include significant myopic or hyperopic shifts. O'Brart et al reported a 1.4-D hyperopic shift over 6 months.[99] Stewart et al reported a slight myopic shift which they attributed to concurrent underlying pathology.[130] This may not be a significant concern to the patient, given the broad improvement in comfort offered by this treatment. Overall, PTK has been shown in a small collection of analyses to be safe and effective for the management of band keratopathy,[66,99,130] but does not show significant advantage over other methods and is associated with high cost, which may continue to limit its use.

4.3. *Keratitis*

Despite identification of a causative organism and modification of medical therapy, progression of the infective process may occur in keratitis. This leads to further stromal infiltration, thinning with potential for perforation and longer-term neovascularization with scar formation.[109] In such cases, surgical intervention in the acute phase can play an important adjunctive role.

Corneal epithelial debridement can improve the penetration of topical antibiotics (Fig. 7). This is usually performed when cultures are obtained. Additionally, debridement removes necrotic tissue containing toxic debris, pathogens, and inflammatory cells, products which could further damage corneal tissue.[109] Debridement of necrotic tissue is an important secondary role of corneal biopsy for investigation of progressive microbial keratitis. A 1 mm margin of macroscopically uninvolved tissue should be included to ensure the active edge of the ulcer is removed and sampled.[6] Surgical debridement should avoid removal of deeper lesions and may cause collateral damage to normal tissue. The discomfort and the resultant irregular astigmatism are poorly tolerated by patients. There is also a significant risk of thinning the cornea further with resulting perforation.

The 193 nm excimer laser has been applied in attempts to sterilize corneal ulcers. Gottsch et al found that the excimer laser could eliminate early infections (<24 hours) of *Fusarium* and *Mycobacterium fortuitum* in a rabbit model; the laser was ineffective, however, in the eradication of more longstanding ulceration.[50] Almost 50% of eyes with *Mycobacterium* infections perforated during laser ablation of depth 150 μm.[68] This technique should be reserved for superficial, well-circumscribed lesions, early in the course of disease.

In early *Acanthamoeba* keratitis, PTK can result in a smoother surface than mechanical dissection because the amoebic focus is in the superficial cornea. Taenaka et al reported a single case where PTK was used to treat *Acanthamoeba* keratitis.[132] They used 640 pulses to ablate 150 μm of the cornea in a 6 mm treatment zone and found that the corneal inflammation subsided quickly after surgical treatment with a final best corrected visual acuity of 20/20. Kandori et al found that PTK completely removed the infectious focus in four treated eyes.[68] They concluded that PTK is safe and effective for the eradication of *Acanthamoeba* keratitis and allows higher drug access to any residual amoebic focus. The advantages of this procedure include direct removal of amoebic cysts, inflammatory cells and necrotic tissues, suppression of tissue scarring, and satisfactory visual outcome without irregular astigmatism.[68]

4.4. *Contact lens–related keratopathy*

The long-term use of contact lenses may damage the ocular surface by mechanical rubbing, hypoxia, and toxic lens solutions. If limbal stem cells are damaged, an invasion of conjunctival epithelium on the corneal surface (conjunctivalization) can occur. This process results in a thickened, irregular, unstable epithelium often with associated inflammation and neovascularization.[21] Ultimately this may lead to persistent corneal defects, corneal ulceration, scarring, and loss of vision.

Mechanical debridement of the conjunctivalized epithelium to encourage corneal re-epithelialization allows adequate corneal epithelial healing to occur from the remaining intact limbus. Dua et al describe a technique using a surgical blade at the slit lamp.[31] Debridement can also be used to prevent migration of conjunctival epithelium onto the

surface of the cornea in acute situations involving partial loss of corneal or limbal epithelium.[31] Visual function and symptoms may improve when there are as little as two clock hours of intact limbus. In contrast, Jeng et al performed debridement of the conjunctival epithelium on one patient in their cohort of focal limbal stem cell deficiency due to soft contact lenses.[65] They found that the conjunctivalized epithelium continued to repopulate the corneal surface faster than the corneal epithelium after the first two debridements and therefore was ineffective.

4.5. *Keratoconus apical scars*

The use of contact lenses in keratoconic patients may be limited by raised nodular subepithelial scars.[79] These apical scars, or proud nebulae, typically 1–2 mm in diameter, are located at, or near, the apex of the cone (Fig. 14). They are usually solitary, but may occur in groups and resemble Salzmann nodular dystrophy macroscopically.[95] The scars may be linked to keratoconus itself, the contact lens/cornea interaction at an irregular surface, or the bearing area of the contact lens being distributed over a small surface at the apex of the cone.[95] Proud nebulae may re-epithelialize after cessation of contact lens wear; the elevated area usually persists, however, and symptoms may return soon after resumption of lens wear.

Superficial keratectomy of proud nebulae may avoid corneal transplantation.[94] In six cases the epithelium was peeled off with fine grooved forceps, and the underlying superficial stroma carefully removed by lamellar dissection with a blade.[94] The patients were given a bandage contact lens for 4–7 days, and normal rigid gas permeable lenses were refit within 4 weeks. The investigators subsequently commented that this technique is crude for the size of lesions, as even using a 2 mm trephine can create an area of excision larger than required.[95] They also found that the wound was invariably irregular and patients reported considerable postoperative pain. Excimer laser ablation of the scar is more precise, but its use is limited by the thickness of the cornea and risk of ectasia.[34,40,95,129]

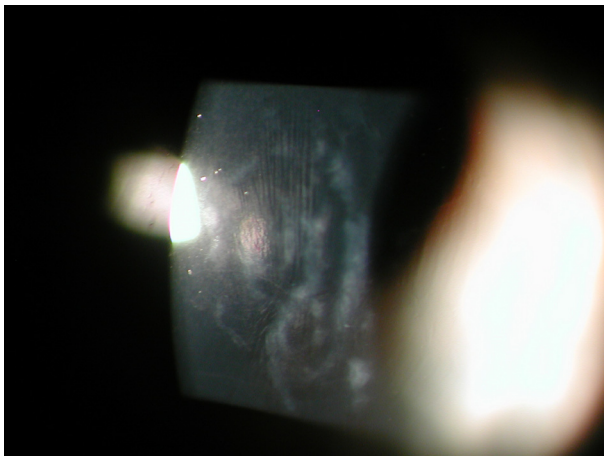

Fig. 14 – Slit lamp view of apical scarring and Vogt's striae in keratoconus.

5. Complications

5.1. *Scarring*

Corneal scarring is the result of a chronic or excessive fibrotic wound repair response and may severely impair the normal function of the cornea and clarity of vision.[33] Scar formation is triggered by tissue damage and results from a complex series of events during wound healing. Growth factors play a major role in scar tissue formation, inducing the synthesis of factors that control cell migration, proliferation, enzyme production, and matrix deposition.[33,76] The final stages of scar formation involve the remodeling of the extracellular matrix, followed by the deposition of new matrix proteins and, finally, contraction of the local tissue into a scar.

When a corneal wound occurs, keratocytes transform into hypercellular myofibroblasts that may later differentiate into wound fibroblasts. These myofibroblasts produce a low level of extracellular matrix containing keratocan and lumican with keratin sulfate chains.[56] The wound fibroblasts, however, produce high levels of collagen to form a highly organized normal extracellular matrix that restores transparency. The synthesis of collagen is mediated by growth factors. Different collagen types and the core proteins of different proteoglycans produce collagen fibrils of specific size and spacing for corneal stromal transparency.[56] The major collagen in the stroma is type I, but collagen type V is also required to initiate assembly of collagen into fibrils.

Transforming growth factors (TGFs), considered the most important of the growth factors in corneal wound healing, are soluble proteins implicated in the myofibroblast transition of fibroblasts and increasing collagen and fibronectin deposited by many different cell types.[33] In addition, TGF-β signaling recruits to the wound site the bone-marrow-derived cells that subsequently express fibronectin, one of the main components of fibrous tissue. Alpha-smooth muscle actin expression by stromal fibroblasts is induced by TGF-β, further increasing contractility and fibrosis.[33] TGF-β may stimulate the corneal edema and opacification that occurs during corneal healing by deposition of the extracellular matrix, inflammatory cell infiltration, and invasion of blood vessels.[76] Modulation of TGF-β–mediated signaling pathways is currently being investigated for the treatment and prevention of debilitating corneal scars.

The repair of corneal wounds after refractive surgery procedures has been of interest since laser surface ablation was introduced in the 1980s. The cornea appears to have only a limited number of wound responses to injury. These include epithelial cell modifications, hypercellular fibrotic stromal scarring, and hypocellular primitive stromal scarring.[27] Basal epithelial thickness changes develop 3 to 7 days after injury and reach completion at approximately 1 month postoperatively. Areas of hypoplasia appear to develop over corneal surface depressions, and conversely, hyperplasia is seen over elevations. In a study of 94 injured corneas, hypercellular fibrotic stromal scars were identified in the first 6 months.[27] After laser surface ablation, wound-repair processes are augmented by epithelial stromal interactions.[27] The resultant hypercellular scar contains a high

density of keratocytes. In corneas with no epithelial–stromal interactions, hypocellular stromal scars are seen.[27] These weak scars remain transparent due to their hypocellularity and lack of myofibroblasts. Poor understanding of and inability to control corneal scarring continues to play a major role in surgical failure and blindness in most of the world today.[33]

5.2. *Recurrent corneal erosion*

Although superficial trauma is the initiating factor in the majority of cases of recurrent corneal erosions, secondary RCE may also follow ocular infection, and refractive or posterior segment surgery. Recurrent erosions also occur following removal of corneal epithelium during vitrectomy. In addition, RCE may manifest after PRK or LASIK. This is paradoxical, because excimer laser PTK is known to be an effective treatment for RCE.[58,135] Superficial damage to the corneal epithelium in LASIK may lead to focal deficiency of basal epithelial structures, the adhesion components that are stimulated by PTK.[135] An undiagnosed epithelial basement membrane dystrophy may be exacerbated by surgery. It is therefore important to minimize epithelial damage during ocular procedures in order to prevent RCE postoperatively.[24]

There are few reports of recurrent erosions after PRK in the literature.[4,58,110] Hovanesian et al administered a patient questionnaire and found that, in fact, symptoms suggestive of mild recurrent erosions are common after PRK.[58] Of the 241 patients who had PRK and returned the survey, 9.1% reported frequent dryness, 4.3% reported frequent eyelid sticking symptoms, and 4.3% reported severe sharp pains. They hypothesized that if the PRK technique involved an epithelial defect larger than the laser treatment zone, symptomatic erosions could occur in the untreated area of epithelium.

After LASIK, RCEs may be caused by corneal neuropathy post flap removal or from epithelial manipulation at the edge of the flap.[24] Ti et al first reported RCE after LASIK and, aside from the epithelial flap complications described earlier, they identified trauma to the corneal surface from the close approximation of the microkeratome as a potential cause of RCE.[135] The poor adherence of the epithelium in patients with this side effect may lead to sloughing, which then may open the potential space within the interface for epithelial cells to migrate from the flap perimeter.[117] Given the high risk of epithelial defects at the edge of the flap, some surgeons advocate the use of a therapeutic contact lens for the first 24–48 hours postoperatively to aid re-epithelialization, but this remains controversial. Other techniques to minimize RCE include the adequate irrigation of the corneal surface immediately before the microkeratome pass and careful manipulation of the epithelial flap. In a large study comparing PRK and LASIK, Hovanesian et al found that symptoms consistent with RCE were less frequent in the LASIK group.[58]

6. Summary

The removal of corneal material has seen evolution in techniques and indications. From mechanical debridement using sharp or dull instruments to the automated ablation of tissue using excimer lasers, corneal debridement can offer patients significant improvements in comfort, quality of vision and cosmesis. The sampling of corneal tissue has also improved diagnosis of ocular surface infections and neoplasia. Adjunctive therapies following corneal debridement modify healing responses in order to maintain normal tissue configuration. The future holds much promise in the further development of such therapies and techniques in the diagnosis and management of anterior segment disease.

7. Method of literature search

The literature was searched using Medline, and articles obtained from bibliographies of these publications (1872–2012). We included references that we considered to have a major contribution to the diagnostic and therapeutic indications and techniques of corneal debridement. The search terms used were *corneal scrape, recurrent corneal erosion, phototherapeutic keratectomy, excimer laser, superficial keratectomy, diamond burr, amoils brush, therapeutic contact lens, stromal puncture, amniotic membrane, keratitis, corneal dystrophy, ocular surface squamous neoplasia, epipolis lasik, corneal scarring, photorefractive keratectomy, conjunctivalization, keratoconus scar, operative corneal edema, corneal healing* and combinations of these terms. The abstracts of relevant non-English articles were also included.

8. Disclosures

The authors have no proprietary interest or research funding to disclose.

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